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Appl. No. 10/085,612  
Reply dated July 7, 2003  
Reply to Office action mailed May 6, 2003

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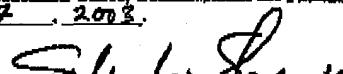
Application No. 10/085,612  
Applicant: Marco Guida, et al.  
Confirmation No. 8119  
Filed: February 26, 2002  
Title: METHODS FOR EVALUATING THE ABILITY TO METABOLIZE  
PHARMACEUTICALS AND COMPOSITIONS THEREFOR  
Art Unit: 1634  
Examiner: Diana B. Johannsen

GROUP 1600

Attorney Docket No.: 4389-5-C1

Commissioner for Patents

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Sandra L. Shancer

#### RESPONSE TO RESTRICTION REQUIREMENT

This paper is being submitted in response to the Office Action dated May 6, 2003, which required  
restriction between claims. Please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims, which begins on page 2 of this  
paper.

Remarks/Arguments begin on page 5 of this paper.

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### Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims:

1.-16. (cancelled)

17.(original) A method of detecting a variant gene having a polymorphism associated with reduced metabolism of a substrate selected from the group consisting of a CYP3A4 substrate, a CYP3A5 substrate and a GSTM1 substrate in an individual, said method comprising:  
(a) obtaining a nucleic acid sample comprising a gene isolated from said individual, said gene selected from the group consisting of a CYP3A4 gene, a CYP3A5 gene and a GSTM1 gene; and,  
(b) detecting the presence or absence in said individual of a polymorphism selected from the group consisting of (i) a substitution of a G nucleotide for an A nucleotide at position -392 of the promoter of said CYP3A4 gene with respect to the start codon of said CYP3A4 gene, wherein the presence of said substitution is associated with reduced CYP3A4 substrate metabolism: (ii) a substitution of a G nucleotide for an A nucleotide at position-147 of the promoter of said CYP3A5 gene, wherein the presence of said substitution is associated with reduced CYP3A5 substrate metabolism; and (iii) a GSTM1 null mutation, wherein the presence of said GSTM1 null mutation is associated with reduced GSTM1 substrate metabolism.

18.(original) The method of Claim 17, wherein said method further comprises, for an individual having one of said nucleic acid sequences, determining whether said individual is homozygous or heterozygous for the polymorphism.

19.(original) The method of Claim 17, wherein the step of detecting is selected from the group consisting of a cDNA assay and a genomic DNA assay.

20.(original) The method of Claim 17, wherein said method comprises the step of digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence comprising said polymorphism and the corresponding wildtype sequence.

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21.(original) The method of Claim 17, wherein said step of detecting comprises amplifying a selected region of the nucleic acid molecule of the individual.

22.(original) The method of Claim 17, wherein said gene is a CYP3A4 gene and wherein said CYP3A4 substrate is selected from the group consisting of cyclophosphamide and BCNU.

23.(original) The method of Claim 17, wherein said gene is a CYP3A5 gene and wherein said CYP3A5 substrate is selected from the group consisting of cyclophosphamide and BCNU.

24.(original) The method of Claim 17, wherein said gene is a GSTM1 gene and wherein said GSTM1 substrate is selected from the group consisting of cyclophosphamide and BCNU.

25.(original) A method for selecting a treatment for a cancer patient, said method comprising:  
obtaining a nucleic acid sample comprising a gene isolated from said individual, said gene selected from the group consisting of a CYP3A4 gene, a CYP3A5 gene and a GSTM1 gene;  
detecting the presence or absence in said individual of a polymorphism selected from the group consisting of (i) a substitution of a G nucleotide for an A nucleotide at position -392 of the promoter of said CYP3A4 gene with respect to the start codon of said CYP3A4 gene, wherein the presence of said substitution is associated with reduced CYP3A4 substrate metabolism; (ii) a substitution of a G nucleotide for an A nucleotide at position -147 of the promoter of said CYP3A5 gene, wherein the presence of said substitution is associated with reduced CYP3A5 substrate metabolism; and (iii) a GSTM1 null mutation, wherein the presence of said GSTM1 null mutation is associated with reduced GSTM1 substrate metabolism; and  
selecting a cancer treatment regime that does not include administration of an anti-cancer agent selected from the group consisting of cyclophosphamide and BCNU if one or more of said polymorphisms are present.

26.(original) The method of Claim 25, wherein said method further comprises, for an individual having one of said polymorphisms, determining whether said individual is homozygous or heterozygous for the polymorphism.

27.(original) The method of Claim 25, wherein the step of detecting is selected from the group consisting of a cDNA assay and a genomic DNA assay.

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28.(original) The method of Claim 25, wherein said method comprises the step of digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence comprising said polymorphism and the corresponding wildtype sequence.

29.(original) The method of Claim 25, wherein said step of detecting comprises amplifying a selected region of the nucleic acid molecule of the individual.

30.(original) A method for selecting a treatment for a cancer patient, said method comprising:  
(a) obtaining a nucleic acid sample comprising a CYP3A4 gene, a CYP3A5 gene and a GSTM1 gene;  
(b) detecting the presence or absence in said individual of the following polymorphisms (i) a substitution of a G nucleotide for an A nucleotide at position -392 of the promoter of said CYP3A4 gene with respect to the start codon of said CYP3A4 gene, wherein the presence of said substitution is associated with reduced CYP3A4 substrate metabolism; (ii) a substitution of a G nucleotide for an A nucleotide at position-147 of the promoter of said CYP3A5 gene, wherein the presence of said substitution is associated with reduced CYP3A5 substrate metabolism; and (iii) a GSTM1 null mutation, wherein the presence of said GSTM1 null mutation is associated with reduced GSTM1 substrate metabolism; and  
(c) selecting a cancer treatment regime that does includes administration of an anti-cancer agent selected from the group consisting of cyclophosphamide and BCNU if none of said polymorphisms are present.

31.(original) The method of Claim 30, wherein said method further comprises, for an individual having one of said polymorphisms, determining whether said individual is homozygous or heterozygous for the polymorphism.

32.(original) The method of Claim 30, wherein the step of detecting is selected from the group consisting of a cDNA assay and a genomic DNA assay.

33.(original) The method of Claim 30, wherein said method comprises the step of digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence comprising said polymorphism and the corresponding wildtype sequence.

34.(original) The method of Claim 30, wherein said step of detecting comprises amplifying a selected region of the nucleic acid molecule of the individual.

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### Remarks/Arguments

#### Election

Applicants elect Group III, claims 17-34, drawn to methods of detecting nucleic acids and selecting disease treatments.

#### Amendments to the Claims

This amendment cancels claims 1-16 that are not elected or traversed by Applicants. Applicants reserve the right to pursue the non-elected subject matter in a subsequent divisional application(s).

#### One month extension of time for response

Applicants note that this response is being filed after the shortened statutory deadline for responding, June 6, 2003, but on or prior to one month following this deadline. Therefore, Applicants respectfully request a one-month extension of time under 37 C.F.R. § 1.136(a), thereby extending the response period to July 7, 2003, the first business day after July 6, 2003. Applicants authorize the Commissioner to deduct the requisite fee for this extension (\$110.00; see 37 C.F.R. § 1.17(a)(2)) from Deposit Account No. 50-1293.

Respectfully submitted,

July 7, 2003

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